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When evolution meets application: the discovery of novel natural products and their potential targets in actinomycetes

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"Nothing in biology makes sense except in the light of evolution" is a famous statement of the evolutionary biologist Theodosius Dobzhansky almost four decades ago. Unquestionably, this statement has had a profound impact on generations of biologists and biochemists and continues to do so. However, the relevance of evolution as the theoretical foundation of biology to the applied aspects of the biological sciences, i.e. biotechnology, has largely been neglected. In this lecture, it will be argued that evolutionary principles can be exploited to generate novel approaches that can guide the discovery of novel natural products with biotechnological implications, as well as novel antibiotic targets. First, two evolutionarily-driven bioinformatics approaches, that we have used for mining the genomes of actinomycetes for novel natural products biosynthetic gene clusters, will be presented. This has lead to the discovery of three previously unrecognized natural products pathways present in *Streptomyces* laboratory strains whose genomes have been publicly available and thoroughly investigated for decades. Second, discovery and validation of a novel antibiotics target in *Mycobacterium* aromatic amino acid biosynthesis, identified after considering principles governing the evolution of enzyme function, will be presented. Overall, the utility of evolutionary principles for applied purposes will be demonstrated, opening new avenues for the development of conceptual frameworks useful for the study of actinomycetes metabolism and its subsequent biotechnological applications.